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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,944	01/22/2001	Andrew R. Marks	61136/JPW/ADM/BJA	3387

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EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,944	MARKS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *April 29, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-6 and 19-21) in Paper No. 7, received April 29, 2003 is acknowledged. The traversal is on the ground(s) that "Applicants ...assert that two or more independent and distinct inventions have not been claimed in the...application because the groups are not independent under M.P.E.P. 802.01. This is not found persuasive because a search of one of the three methods would not be a complete search of the remaining methods. Group III drawn to a product is separate and distinct by virtue of different classification. The argument that a search encompassing Groups I-IV is not found persuasive for the reasons set forth in the restriction requirement (Paper No. 6, mailed March 18, 2002).

As to the question of burden of search, the claims of four different groups are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to.

The requirement is therefore made FINAL.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims

limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

2. Claims 1-21 are pending.

Claims 7-18, drawn to

Claims 22-24 have been cancelled.

Specification

3. The disclosure is objected to because of the following informality: on page 10, line 24 a sentence does not end with a period. Hence it is not clear if additional text is missing.

Correction is required.

Claim Objections

4. Claims 19 and 21 are objected to because of the following informality: they both reference non-elected claims 7 and 9. Correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-6 and 19-21 are drawn to a method of treating a subject with a cardiovascular disease with a therapeutically effective amount of chemical compound, novel structural and functional analog or homolog thereof. The specification does not reasonably provide enablement for the administration of any chemical compound, novel structural and functional analog or homolog. Furthermore, the specification broadly describes these structural and functional analog or homolog as compounds that have structure similar to a chemical compound but differing from it in respect to a certain component or components and maybe with the addition of a constant element, see bridging paragraph of pages 16 and 17. There is no guidance as to how to make these divergent molecules. The products of these homologs and analogs, may possess function that is not commensurate with the functions alleged by the method claims. The broadly described molecules may not maintain the activities proposed in the specification. In the absence of an established role of the broad chemical compounds and novel structural and functional analog or homolog thereof in targeted treatment of cancer and cardiovascular diseases it is impossible to predict what if any therapeutic effect the administration of any of these molecules would have in the said methodologies. There is no data or established precedent presented that would lead one of skill in the art to believe that functional homologs or analogs and the like would

be able to function as the methodology dictates, i.e. inhibiting tumor metastasis. It is clear from the figures that the administration of rapamycin *in vitro* and *in vivo* produced effects such as significant inhibition of smooth muscle cells (SMC) migration, however there is insufficient evidence of record providing that the broadly listed chemical compound and homologs and analogs, thereof would yield such a result. This analysis sustains the Examiner's position that there appears to be no nexus between Applicants' broadly claimed method of treating a subject with cardiovascular disease and tumor metastasis by administering undefined chemical compounds.

The selection and development of such therapeutics is art known to be highly unpredictable. The specification exemplifies no examples of the effective use of arbitrary chemical compounds and derivatives as a therapeutic pharmacological agent for the treatment of any particular cancer or any specific cardiovascular disease. This reasonably conjures the question as to how selective the use of the claimed composition clearly is or would be. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the claimed method employing a chemical compound as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. There is no guidance as to how the instant molecules can be employed as therapeutic nor a basis to predict their efficacy in any therapy. Additionally, it would require undue experimentation of one skilled in the art to apply a method of treatment to a human based on the teachings of a method of treating

a non-human animal. Without such guidance, the changes which must be made in the compounds, chemical compounds and analogs and homologs, thereof, which results in effective therapeutic agents is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-6 and 19-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "cell" is vague and indefinite in claim 1. It is not clear what type of cell is affected by the increase of the intracellular cyclin-dependent kinase inhibitor p27 activity. Furthermore, it is not clear if this cell is isolated, created by nature or man made. Accordingly, the metes and the bounds cannot be determined.

b. Claims 3, 5, 19 and 21 are vague and indefinite in the recitations "compound" and "chemical compound". The metes and bounds of the claim cannot be determined. A "compound" can be anything, such as a peptide, an organic molecule, an inorganic molecule, a DNA fragment, a plastic, a carbohydrate, etc. Applicant's attention is directed to Ex Parte Tanksley (26 USPQ2d 1384) wherein the Board noted that under 35 U.S.C. 112, second paragraph, the claims must be so definite as to allow the comparison with the available art and must also make it possible for the public to

determine from the claim what it encompasses. Hence, it would be difficult for one to know if the patented claimed was being infringed.

c. The phrase "alleviating the subject's cardiovascular disease" in claim 3 is vague and indefinite. It is not clear from the claim how the subject's cardiovascular disease would be lessened or relieved. The metes and the bounds cannot be determined absent an accurate description.

d. Claims 19 and 21 are vague and indefinite in the recitation "therapeutically effective amount" when the claims fail to state the function, which is to be achieved. *In re Frederiksen*, 213 F 2d 547, 102 USPQ 35 (CCPA 1954). Moreover, it not apparent from the claims what amount is deemed effective in having an influence the treatment of cardiovascular disease.

e. The terms "novel structural and functional analog" and "homolog" in claims 19 and 21 are vague and indefinite. It is not clear what is meant by the terms. It is not clear how similar or different the analogs and homologs are in comparison to the chemical compounds capable of treating cardiovascular disease and inhibiting tumor metastasis. Accordingly, the metes and bounds of the claimed "analog" and "homolog" are unclear.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Horiuchi et al. (Molecular Human Reproduction 5(2): 139-145, February 1999). Horiuchi discloses a method of inhibiting cultured myometrial and leiomyomal tumor smooth muscle cells (SMC) by heparin treatment with the concomitant induction of cyclin-dependent kinase inhibitor p27, see abstract; page 139, column 2, first paragraph; page 142, column 2, last sentence of bridging paragraph; page 143, column 2, last sentence; Figure 5; and page 144, column 1, first paragraph. It is reasonable to conclude that concurrent with the inhibition of cell growth is the prevention of cell migration. Moreover, inherently the increase of the cyclin-dependent kinase inhibitor p27 is due to the increase of C3 exoenzyme activity.

11. Claims 1, 3-6 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/65939/ IDS reference from Paper number 8 (23 December 1999). This WO document discloses methods for modulating, i.e. enhancing the activity of a p27(Kip1).FKBP-12 complex, see page 9, lines 24 and 25. Upregulation of the cyclin kinase inhibitor p27(Kip1) leads to cell cycle arrest and results in decrease cell proliferation, see page 7, lines 6-8. The disclosed invention provides a method for treatment or prevention of various diseases and disorders, such as those related to organ transplantation, tumor spread, autoimmune diseases and atherosclerosis by administration of a therapeutic compound that modulates, i.e. promotes p27(Kip1).FKBP-12, see page 27, lines 10-29; page 33, lines 3-5. It is reasonable to

conclude that concurrent with the inhibition of cell growth is the prevention of cell migration. Moreover, inherently the increase/enhancement of the cyclin-dependent kinase inhibitor p27 is due to the increase of C3 exoenzyme activity.

12. Claims 1-4, 6, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/03508/ IDS reference from Paper number 8 (28 January 1999). WO 99/03508 discloses that the overexpression of p27 arrests the growth of 293 cells and vascular smooth muscle cells (VSMC), see page 21, lines 6-20; page 23, lines 11 and 12; and bridging sentence of pages 28 and 29. This WO document also discloses a method for providing a gene composition which expresses p27 in a therapeutically effective amount to a patient with a vascular proliferative disease, such as atherosclerosis, angiogenesis and restenosis, see page 4, lines 7-21; page 10, line 11-page page 12, line 2. It is reasonable to conclude that concurrent with the inhibition of cell growth is the prevention of cell migration. Moreover, inherently the increase/enhancement of the cyclin-dependent kinase inhibitor p27 is due to the increase of C3 exoenzyme activity.

13. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Poon et al. (J. Clin. Invest. 98(10): 2277-2283, November 1996/ IDS reference, exhibit 9 from Paper number 4). Poon discloses rapamycin inhibits VSMC proliferation and migration, see abstract.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
February 21, 2003